

Notice of Allowability	Application No.	Applicant(s)	
	09/555,026	MUKAI ET AL.	
	Examiner	Art Unit	
	Frederick Krass	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to the amendment dated July 5, 2006.
2. ☒ The allowed claim(s) is/are 32-50.
3. ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) ☐ All b) ☒ Some* c) ☐ None of the:
 1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

* Certified copies not received: 11/279147.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
 - (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
 - 1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
 - (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

- | | |
|--|---|
| <ol style="list-style-type: none"> 1. <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) 2. <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) 3. <input type="checkbox"/> Information Disclosure Statements (PTO-1449 or PTO/SB/08),
Paper No./Mail Date _____ 4. <input type="checkbox"/> Examiner's Comment Regarding Requirement for Deposit
of Biological Material | <ol style="list-style-type: none"> 5. <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) 6. <input checked="" type="checkbox"/> Interview Summary (PTO-413),
Paper No./Mail Date <u>07/20/06</u> . 7. <input checked="" type="checkbox"/> Examiner's Amendment/Comment 8. <input checked="" type="checkbox"/> Examiner's Statement of Reasons for Allowance 9. <input checked="" type="checkbox"/> Other <u>Drawings (5/23/00) approved</u>. |
|--|---|

Frederick Krass
 Primary Examiner
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Priority

Upon review of this case for allowance, the examiner noted that there is no copy of foreign priority document 11/279147 in his electronic ("E-Dan") file. (This is noted on Form PTOL-37 (Notice of Allowability) as well).

Examiner's Amendment

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Mr. Garrett on 07-20-2006.

The following changes have been made:

- 1) As the first line of the specification there has been inserted:

--- This application is a 371 of PCT/JP00/01722, filed 03/21/2000 ---

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2) In the specification, page 2, line 24, "cilostazol" has been deleted and replaced with --- certain pharmaceutical agents ---¹

3) Claim 47, last two lines, the phrase "and rapid release powders or tablets containing cilostazol" has been deleted in its entirety.

Reasons for Allowance

The following is an examiner's statement of reasons for allowance:

Due to the extended nature of the prosecution in this case (involving multiple examiners), a brief review of the rationale for allowing this case would appear appropriate.

The instant claims are drawn to cilostazol preparations for oral administration (powders, granules, pills, tablets or capsules) which are able to dissolve at the lower portion of the human digestive tract.² These orally administrable preparations contain, as the active ingredient, a fine powder of cilostazol which has been incorporated into a surfactant as dispersing and/or solubilizing agent. The fine powder has an average particle size of from 2 to 10um.

Significantly, no prior art of record discloses either 1) the instantly claimed particle sizes or 2) incorporation of cilostazol into a surfactant separately, let alone both features simultaneously. Indeed, the two closest references of record not only fail to disclose

¹ While Japanese Publication Number 07-291869 clearly discloses fine powders of diphosphonic acid esters having improved bioavailability, it makes no apparent mention of cilostazol. (The cyanophenyl carbamoyl compounds specified therein are not even remotely structurally related to cilostazol).

² The term "lower portion of the digestive tract" is clearly synonymous with the term "large intestine", as defined at page 5, lines 5-10 of the instant specification.

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incorporation into surfactants, but also have disclosure dates later than that of the instant application. See US 2005/0255155, newly cited on the Form PTO-892 and discussed in the “Technological Background” section infra; see also USP 6,825,214 (which furthermore only discloses a minimum specified particle size of 15um).

Conversely, Applicant has convincingly demonstrated that cilastazol having reduced particle size (10 um or less) when incorporated into a surfactant unexpectedly exhibits greatly improved bioavailability (up to a twenty-fold increase: see page 64, lines 4-8) due to an increased dissolution rate in the lower intestine. This has been factually demonstrated in extensive detail throughout the instant working examples and is reinforced by the Rule 132 Declaration by Tadashi Mukai, dated April 9, 2003. The significance of these results – unexpected both in kind and degree – is summarized by Applicant’s discussion bridging the bottom of page 66 to the top of page 67. As noted therein, the unique pharmacokinetics of cilostazol require the instantly claimed combination of both low particle size and incorporation into a surfactant in order to obtain this unexpected bioavailability. (Given the state of the prior art as discussed supra, the comparative showings made in the instant working examples against preparations having a particle size of 20um are viewed as probative since they are based on the closest available prior art at the time of filing (JP Pat. Pub. No. 10-67657, cited at the bottom of page 3 of the instant specification)).

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue

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fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Technological Background Material

The following reference is made of record as being considered pertinent to applicant's disclosure, but is not relied upon since it is not available as "prior art" by virtue of its later publication date.

US 2005/0255155 discloses pharmaceutical compositions comprising cilastozol having a particle size of 10um or less. The existence of this disclosure is viewed as further corroboration of the fact that cilastozol having a particle size of 10um or less was not known prior to the filing date of the instant application.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frederick Krass whose telephone number is (571) 272-0580. The examiner can normally be reached on Monday-Friday from 9:30AM to 6:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached at (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Frederick Krass
Primary Examiner
Art Unit 1614

